Stereochemistry of Formation of (2—4η)-PdCl Complexes from Deuterio-substituted 1-Acetyl-4-t-butylcyclohex-1-enes

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Summary The loss of ^1H and ^2H during the formation of (2—4η)-PdCl compounds from deuterio-substituted 1-acetyl-4-t-butylcyclohex-1-enes shows little stereoselectivity and is compatible with a mechanism of formation which involves an initial palladium-assisted enolisation of the enone.

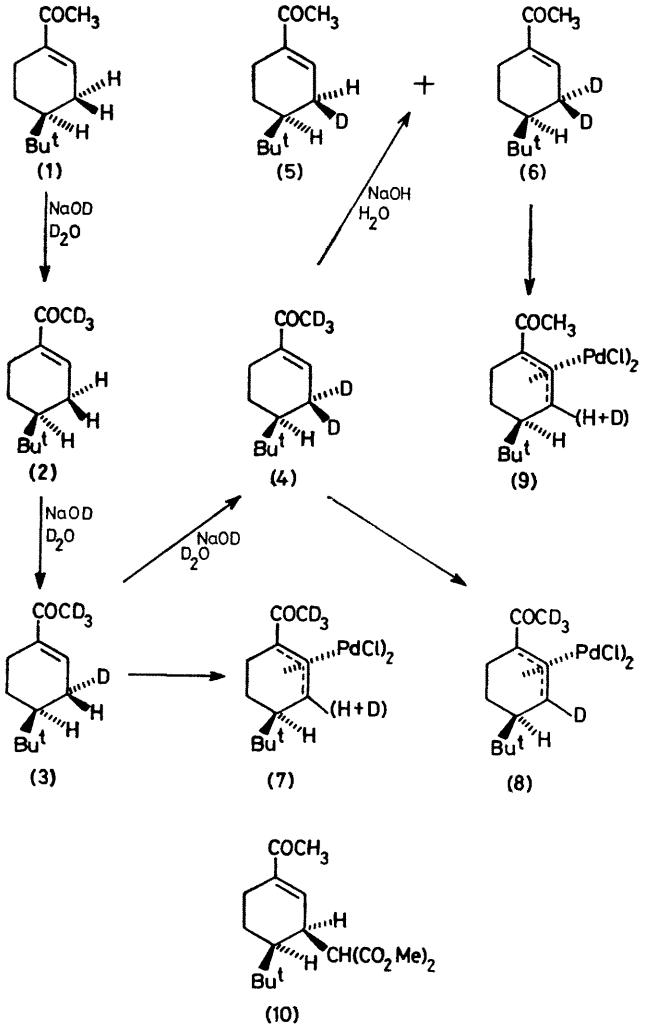
THE preceding communication[1] showed that the formation of α-(4—6η)-PdCl derivatives from steroidal 4-en-3-ones involved a highly stereoselective loss of the 6β-proton or -deuteron. In order to ascertain whether this loss was due to a steric requirement for proton loss *trans* to the incoming metal or to the much greater reactivity of the pseudo-axial 6β-proton in enolisation reactions, a more flexible system was investigated.

1-Acetyl-4-t-butylcyclohex-1-ene (**1**) was treated with NaOD and D_2O in dioxan under conditions such that mixtures rich in the kinetically controlled products (**3**), the pentadeuterio-derivative (**4**), and (by back exchange with NaOH and H_2O) the species (**5**) and (**6**), were formed (Scheme). The stereochemistry of (**3**) was assigned on the basis of spectroscopic and kinetic data.[2] The series of deuterio-mixtures (detailed in the Table) were then treated separately with Na_2PdCl_4 in dry tetrahydrofuran (THF).

TABLE.

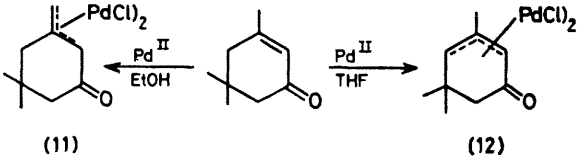
Reactants: % of reactants containing < 3 D atoms	(2)	(3)	(4)	Product ratio (7) H:D	Calculated product ratios[a]: All α-loss	All β-loss	No stereoselectivity
2	35	53	10	3·2:1[b]	1:1·1	3·7:1	1·7:1
26	37	31	6	3·0:1	2·3:1	7·1:1	3·6:1
	(1)	(5)	(6)	(9) H:D			
	11	47	42	1:1·7	1:1·1	1:3·8	1:1·9

[a] Calculated on the basis that base-catalysed exchange gives a 3·8:1 preference for 3β-H over 3α-H exchange. Thus, *e.g.*, (3) contains 21% of the epimeric 3α-deuterio derivative. [b] Average of two determinations.



A single allylpalladium stereoisomer was isolated from the reaction mixtures and assigned the stereochemistry with the palladium atom on the face of the ring *trans* to the t-butyl group (designated β), (*cf.* ref. 2). Assignments were made on the basis of n.m.r. evidence and the formation of a single α-malonic ester derivative (**10**) on reaction of the π-allyl complex with malonate ion.[3] Nucleophilic substitution of π-allyl palladium complexes is known to occur from the opposite face of the molecule to that containing the palladium atom.[4]

Scrambling of deuterium within the allyl complex was monitored by integrating the signal for acetyl methyl compared with t-butyl methyls. In all cases, exchange was < 20% into the acetyl methyl group suggesting that exchange of ring protons would be very small indeed in view of the much greater rate of exchange of the former protons.[2] The amount of deuterium substituted at C-3 was estimated by comparison of the integrals of the signals at δ 6·02, due to H-2, with those at δ 5·37, due to H-3.



A mixture rich in the pentadeuterio-species (**4**) was treated with Na_2PdCl_4 in dry THF. The allyl complex formed was predominantly (**8**). Only a very small amount of the ^1H-4 isomer (< 5%) was obtained arising from incorporation of protons from the solvent. A series of reaction mixtures rich in (**3**) and (**5**) and (**6**) were then treated under the same anhydrous conditions. The ratios of ^1H to ^2H at C-3 in the products were compared with values calculated assuming stereospecific loss of β-proton or deuteron (*cis* to the approaching metal), stereospecific α-loss (*trans* to the approaching metal), and complete non-stereoselective loss of α- and β-protons (Table).

The possibility of a stereospecific loss of the α-proton, *trans* to the incoming metal, is clearly eliminated. The results in the first line of the Table, which are probably the least susceptible to errors, suggest a preference for loss of the β-deuteron, whereas the other results suggest no discrimination between α- and β-loss. The base-catalysed enolisation of (**1**) has been shown to involve a 3·8:1 preference for exchange of 3β-H over 3α-H and thus the results are compatible with a mechanism which involves a metal-assisted enolisation of the enone as was suggested by the steroidal reaction of ourselves[1] and McQuillin.[5]

The involvement of a metal-catalysed enolisation as a first step in allylpalladium complex formation could mean that the direction of allyl formation be dependent on external conditions, *e.g.* of solvent and temperature. We report an example of such a solvent modification of products. Reaction of isophorone with Na_2PdCl_4 in dry THF gave the endocyclic isomer (**12**) as the sole product

whereas reactions in ethanol gave lower yields of mixtures of (**12**) and the exocyclic isomer (**11**), in which (**11**) predominated.[6]

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